

This listing of claims will replace all prior versions, and listings, of claims in the application:

**LISTING OF CLAIMS:**

1. - 24. (Canceled)

25. (Currently Amended) A composition comprising:

- i) a granulated preparation comprising a complex between an estrogen and a cyclodextrin; and
- ii) optionally, one or more excipients,

the composition having a stability such that said estrogen is in an amount of at least 85% w/w in relation to the initial content of said estrogen after storage for 12 months at 40°C and 75% relative humidity (RH).

26. (Canceled)

27. (Canceled)

28. (Original) The composition according to claim 25, wherein the estrogen is in an amount from about 0.002 % w/w to 2% w/w.

29. (Original) The composition according to claim 25, wherein the estrogen is in an amount from about 0.004% w/w to 0.2% w/w.

30. (Original) The composition according to claim 25, wherein the estrogen is ethinyl estradiol and the cyclodextrin is  $\beta$ -cyclodextrin, the ethinyl estradiol is in an amount relative to the ethinyl-estradiol- $\beta$ -cyclodextrin complex of from about 5 % w/w to 20 % w/w.

31. (Original) The composition according to claim 25, wherein the estrogen is ethinyl

estradiol and the cyclodextrin is  $\beta$ -cyclodextrin, the ethinyl estradiol is in an amount relative to the ethinyl-estradiol- $\beta$ -cyclodextrin complex of from about 8% w/w to 15% w/w.

32. - 36. (Canceled)

37. (Currently Amended) A method for improving the stability of an estrogen in a pharmaceutical composition that comprises an estrogen and one or more excipients in a granulate preparation, the which method comprises ~~the steps of~~:

- i) forming a complex between said estrogen and a cyclodextrin; ~~and~~
- ii) providing the complex in a granulator;
- iii) introducing a granulating liquid into the granulator; and
- iv) mixing the granulator contents under granulation conditions ~~the said complex~~ with the one or more excipients to provide a granulate, such that the relative humidity of the ~~final~~ granulate does not exceed 60%, as determined at a temperature between 20°C and 40°C,

provided that, when the one or more excipients comprises polyvinylpyrrolidone, it is present in an amount of at most 2% w/w.

38. (Canceled)

39. (Original) The method according to claim 37, wherein the one or more excipients comprises polyvinylpyrrolidone in an amount of at most 1% w/w

40. (Original) The method according to claim 37, wherein the one or more excipients comprises polyvinylpyrrolidone in an amount of at most 0.5% w/w.

41. (Original) The method according to claim 37, wherein the one or more excipients comprises polyvinylpyrrolidone in an amount of at most 0.2% w/w.

42. (Currently Amended) A process for manufacturing a granulate preparation

comprising a complex between an estrogen and a cyclodextrin, ~~wherein the processing of the granulate preparation comprises the steps of~~ which comprises:

- i) loading the complex, optionally further one or more therapeutically active agent(s) and one or more excipients into a granulator;
- ii) applying a granulating liquid onto the loaded complex and the one or more excipients, and
- iii) granulating under granulation conditions so as to obtain granules having a relative humidity not exceeding 60%, as determined at a temperature between 20°C and 40°C.

43. (Original) The process according to claim 42, wherein the complex and the optionally further one or more therapeutically active agent(s) are provided as individual agent(s) without being pre-mixed with excipients.

44. (Original) The process according to claim 42, wherein the relative humidity of the granulate preparation does not exceed 55%, as determined at a temperature between 20°C and 40°C.

45. (Original) The process according to claim 42, wherein the relative humidity of the granulate preparation does not exceed 45%, as determined at a temperature between 20°C and 40°C.

46. (Original) The process according to claim 42, wherein the relative humidity of the granulate preparation does not exceed 40%, as determined at a temperature between 20°C and 40°C.

47. (New) The composition according to claim 25, provided that when the granulated preparation comprises polyvinylpyrrolidone it is present in an amount of at most 2% w/w.

48. (New) The composition according to claim 25, wherein the composition

comprises one or more excipient(s) which is/are selected from the group consisting of starch, cellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose and maltodextrin.

49. (New) The composition according to claim 25, wherein the estrogen is selected from the group consisting of ethinyl estradiol, estradiol, estradiol sulfamates, estradiol valerate, estradiol benzoate, estrone, estrone sulfate and mixtures thereof.

50. (New) The composition according to claim 49, wherein the estrogen is ethinyl estradiol.

51. (New) The composition according to claim 25, wherein the cyclodextrin is selected from the group consisting of  $\alpha$ -cyclodextrin,  $\beta$ -cyclodextrin,  $\gamma$ -cyclodextrin and alkylated or acylated derivatives thereof.

52. (New) The composition according to claim 25, wherein the cyclodextrin is  $\beta$ -cyclodextrin or an alkylated or acylated derivative thereof.

53. (New) The composition according to claim 25, wherein the estrogen is in an amount relative to the cyclodextrin such that a molar ratio between the estrogen and the cyclodextrin is from about 2:1 to 1:10.

54. (New) The composition according to claim 25, further comprising one or more therapeutically active agent(s).

55. (New) The composition according to claim 54, wherein the one or more therapeutically active agent(s) is a progestogen.

56. (New) The composition according to claim 56, wherein the progestogen is selected from the group consisting of drospirenone, levonorgestrel, norgestrel, gestodene,

dienogest, cyproterone acetate, norethisterone, norethisterone acetate, desorgestrel, and 3-keto-desorgestrel.

57. (New) The composition according to claim 56, wherein the progestogen is drospirenone.

58. (New) The composition according to claim 57, wherein drospirenone is in micronized form.

59. (New) The composition according to claim 58, wherein drospirenone is in an amount from about 0.4 % to 20% w/w.

60. (New) The composition according to claim 25, wherein the complex is micronized.

61. (New) The composition according to claim 25, further comprising an antioxidant.

62. (New) The composition of claim 25, wherein the granulated preparation has a mean particle size of at least about 100  $\mu\text{m}$ .

63. (New) The method according to claim 37, provided that the one or more excipient(s) is/are selected from the group consisting of starch, cellulose, hydroxypropylcellulose, hydroxypropylmethylcellulose and maltodextrin.

64. (New) The process according to claim 42, provided that, when the granulated preparation comprises polyvinylpyrrolidone, it is present in an amount of at most 2% w/w.

65. (New) The method according to claim 42, provided that the one or more excipient(s) is/are selected from the group consisting of starch, cellulose,

hydroxypropylcellulose, hydroxypropylmethylcellulose and maltodextrin.

**66. (New)** The process according to claim 42, wherein the estrogen is selected from the group consisting of ethinyl estradiol (EE), estradiol, estradiol sulfamates, estradiol valerate, estradiol benzoate, estrone, estrone sulfate and mixtures thereof.

**67. (New)** The process according to claim 66, wherein the estrogen is ethinyl estradiol.